1647

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

GOLDSPINK et al.

Serial No. 09/852,261

Filed: May 10, 2001

Title: REPAIR OF NERVE DAMAGE

Atty Dkt. 117-351
C# M#
Group Art Unit: Unassigned
Examiner: Unassigned
Date: August 27, 2002

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Assistant Commissioner for Patents
Washington, DC 20231

Sir:

RESPONSE/AMENDMENT/LETTER

This is a response/amendment/letter in the above-identified application and includes an attachment which is hereby incorporated by reference and the signature below serves as the signature to the attachment in the absence of any other signature thereon.

Fees are attached as calculated below:

Total effective claims after amendment **0** minus highest number previously paid for **20** (at least 20) = 0 x $ 18.00	$	0.00
Independent claims after amendment **0** minus highest number previously paid for **3** (at least 3) = 0 x $ 84.00	$	0.00
If proper multiple dependent claims now added for first time, add $280.00 (ignore improper)	$	0.00
Petition is hereby made to extend the current due date so as to cover the filing date of this paper and attachment(s) ($110.00/1 month; $400.00/2 months; $920.00/3 months)	$	0.00
Terminal disclaimer enclosed, add $ 110.00	$	0.00
☐ First/second submission after Final Rejection pursuant to 37 CFR 1.129(a) ($740.00) ☐ Please enter the previously unentered , filed ☐ Submission attached	$	0.00
Subtotal	$	**0.00**
If "small entity," then enter half (1/2) of subtotal and subtract ☐ Applicant claims "small entity" status. ☐ Statement filed herewith	-$	0.00
Rule 56 Information Disclosure Statement Filing Fee ($180.00)	$	0.00
Assignment Recording Fee ($40.00)	$	0.00
Other: Request Under Rule 221(b)		**0.00**
TOTAL FEE ENCLOSED	$	**0.00**

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Account No. 14-1140. A duplicate copy of this sheet is attached.

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NIXON & VANDERHYE P.C.
By Atty: B. J. Sadoff, Reg. No. 36,663

Signature: 

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DmT
9-6-02

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For: REPAIR OF NERVE DAMAGE

* * * * * * * * * * * *

Assistant Commissioner for Patents
Washington, DC 20231

August 27, 2002

Sir:

REQUEST UNDER RULE 221(b)

Pursuant to 37 CFR §1.221(b), applicants hereby request a corrected or revised patent publication to correct the following described mistakes in the original publication No. US 2002/0083477A1 (published June 27, 2002, hereinafter "the published application"), made by the U.S. Patent Office, which should be apparent from the Patent Office records.

The following corrected numbered paragraphs correspond with numbered paragraphs of the published application. Changes/corrections are shown in the attached marked up copy of these paragraphs wherein deleted terms and phrases are bracketed and underlined terms and phrases are to be added.

CORRECTED TEXT

[0003] The terminology for the IGF-I splice variants is based on the liver isoforms (Chew et al, 1995) and has not fully evolved to take into account those produced by non-liver tissues The latter are controlled to some extent by a different promoter (promoter 1) to the liver IGP-I isoforms, which respond to hormones and are under the control of promoter 2 (Layall, 1996)

[0005] These are alternative splice variants. Exons 1 and 2 are alternative leader exons (Tobin et al, 1990; Jansen et al, 1991) with distinct transcription start sites which are differentially spliced to common exon 3. Exons 3 and 4 code for the mature IGF-I peptide (B, C, A and D domains) as well as the first 16 amino acid of the E domain. Exons 5 and 6 each encodes an alternative part of a distinct extension peptide, the E domain. This is followed by the termination codons of precursor IGF-I, 3' untranslated regions and poly(A) addition signal sites (Rotwein et al, 1986). A further difference between the two isoforms is that MGF is not glycosylated and is therefore smaller. It has also been shown to be less stable. It may thus have a shorter half-life.

[0055] Preferably, MGFs of the invention comprise exons 3, 4, 5 and 6 or equivalent sequences. Optionally, they may include exons 1 and/or 2, or equivalent sequences as well.

[0074] The sequence of the polypeptides of SEQ ID NOs. 2, 4 and 6 and of the allelic variants and species homologues can be modified to provide further polypeptides of the invention.

[0183] Nerve regeneration was observed in samples from all groups In particular, a continuous cord of Schwann cells was seen to extend between proximal and distal nerve

ends, showing similar quantities for MGF, IGF1 and control groups. These results indicate that the conduit or the matrix used in these experiments did not impede regeneration. When axonal regeneration was examined, the results were very different from those seen with Schwann cells staining. Indeed, axonal regeneration was scarce in the conduits filled with alginateand control plasmid (i.e. no cDNA insert), with few axons extending into the distal nerve stump. Addition of IGF1 cDNA-plasmid produced an increased amount of axonal regeneration, with a moderate number of fibres reaching into the distal nerve stump. Regeneration was further enchanced when MGF cDNA-plasmid was added to the alginate matrix. In these conduits, a vigorous regeneration was seen throughout the width of the nerve, with numerous axons extending well into the distal nerve stump. No quantification was attempted, but the disparity of the staining was so considerable as to be able to determine without difficulties the difference between groups

REFERENCES

The following is a list of the corrections of the published application wherein basis in the originally-filed application for the correction is noted in parenthesis.

Paragraph 0003, line 2 "river" was originally "liver" (line 24 on page 1);

Paragraph 0005, line 8 "Thtis" was originally "This" (line 12 on page 2);

Paragraph 0055, line 2 "on" was originally "or" (line 1 on page 10);

Paragraph 0074, line 1 "ED" was originally "ID" (line 17 on page 13);

Paragraph 0183, line 12 "IFGI" was originally "IGFI" (line 10 on page 36).

The Commissioner is authorized to charge the undersigned's deposit account #14-1140 in whatever amount is necessary for correction of the publication however no fee is believed required as these errors were the result of Patent Office mistake.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

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